

REMARKS

Claims 1-10 are currently pending in this application. In response to the restriction requirement mailed on July 25, 2006, applicants note that they had elected to prosecute Group I (claims 1-10). In the Office Actions that have issued since then, the Examiner states that claims 1-9 are pending, with claim 10 being withdrawn. Applicants ask for clarification with regard to this matter. Applicants have cancelled claims 11-14 as being drawn to non-elected subject matter (Group II) and reserve the right to file for and obtain claims directed to this subject matter in divisional or continuing applications claiming priority and benefit herefrom, or from a related application, under 35 U.S.C. § 120.

Rejection under 35 USC 103(a):

The Examiner rejected claims 1-9 under 35 U.S.C. § 103(a), as allegedly unpatentable over Garvey *et al.* (US 5,824,669) (“Garvey”) in view of Carling *et al.* (US 5,674,860) (“Carling”) and Palmer (US 5,208,226) (“Palmer”). Applicants traverse.

The Supreme Court addressed the issue of obviousness in *KSR International Co. v. Teleflex Inc.*, 127 S. Ct. 1727 (2007), wherein the Court stated that the *Graham v. John Deere Co. of Kansas City*, 383 U.S. 1 (1966), factors still control an obviousness inquiry. Those factors, (1) the scope and content of the prior art; (2) the differences between the prior art and the claims; (3) the level of ordinary skill in the pertinent art; and (4) objective evidence of non-obviousness, are discussed in more detail below.

(1) Scope and content of the prior art / (3) Level of skill in the art

Carling is directed entirely to the specific combination of formoterol (long-acting β 2-agonist) and budesonide (a glucocorticoid; a corticosteroid refers to both glucocorticoids and mineralocorticoids). Palmer is directed entirely to the combination of salmeterol (long-acting β 2-agonist) and beclomethasone dipropionate (a corticosteroid). One of skill in the art reading Carling and Palmer would notice that combinations of long-acting β 2-agonists and corticosteroids may be promising in the treatment of respiratory disorders.

Garvey is noticeably different from Carling and Palmer – Garvey relates specifically to nitrosated and nitrosylated compounds for treating respiratory disorders. In particular, Garvey suggests attaching a NO or NO₂ group to known compounds identified in a general list. Garvey

claims, “[t]he present invention is based on the discovery by the inventors that it is possible to directly or indirectly link an NO or NO₂ group or a group which stimulates the endogenous production of NO or endothelium-derived relaxing factor (EDRF) in vivo, to a steroid, a β -agonist, an anticholinergic, a mast cell stabilizer or a phosphodiesterase (PDE) inhibitor and that the resulting compound has beneficial therapeutic effects of both a steroid, a β -agonist, an anticholinergic, a mast cell stabilizer, or PDE inhibitor and an NO donor or stimulator (column 2, lines 55-62).” One of skill in the art reading Garvey would learn that NO-/NO₂-modified β 2-agonists, NO-/NO₂-modified anticholinergic agents, NO-/NO₂-modified mast cell stabilizers or NO-/NO₂-modified PDE inhibitors may be promising in the treatment of respiratory disorders.

(2) Differences between the prior art and the claims

There is no nexus between the disclosures of Carling, Palmer and Garvey and that of the presently claimed invention. Carling and Palmer disclose combinations of β 2-agonists and corticosteroids and Garvey discloses general nitrosation and nitrosylation of known asthma compounds (β 2-agonists, anticholinergic agents, mast cell stabilizers and PDE inhibitors). In contrast, the presently claimed invention relates to the combination of long-lasting anticholinergics and long-lasting β -mimetics (or β -agonists). None of the above-cited references alone or together combines anticholinergics with β -agonists as a combination treatment for respiratory ailments.

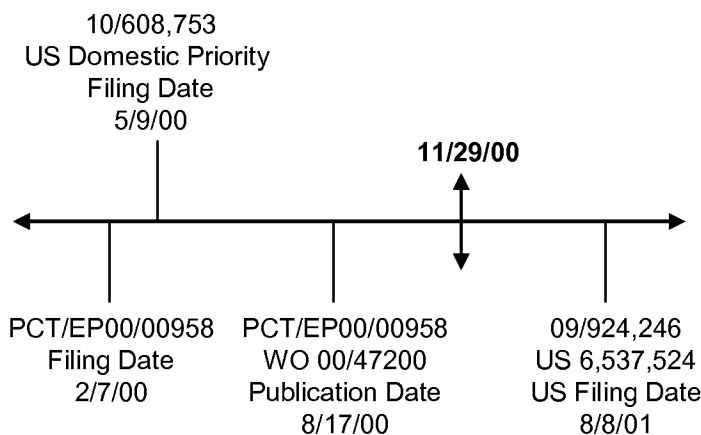
(4) Objective evidence of non-obviousness

Carling, Palmer, and Garvey do not disclose the unexpected result of this invention, that is, the combination of long-lasting anticholinergics and long-lasting β -mimetics provides a synergistic effect. For example, the addition of an anticholinergic to a betamimetic acts synergistically to reduce the cardiac side effects of the betamimetic. See Tables on pages 16-21 of the specification. In addition, applicants previously provided a Declaration of Alexander Walland in the parent case to demonstrate the synergistic effects of tiotropium bromide with salmeterol hemisulfate (copy attached). As such, applicants have provided the necessary objective evidence of non-obviousness.

The above Graham factor analysis demonstrates that an obviousness inquiry fails and the rejection for obviousness should be withdrawn.

Rejections under 35 USC 102(e):

Claims 1-6, 8-9 stand rejected under 35 U.S.C. § 102(e) as being anticipated by Hassan et al. (US 6,537,524) (“Hassan”). Applicants traverse because Hassan does not qualify as a 102(e) reference. Applicants refer to the following diagram:



and to section 706.02(f)(1)(I)((C))(3) of the MPEP. Hassan is a continuation of international application PCT/EP00/00958, filed on February 7, 2000. The international application was filed prior to November 29, 2000 and thus, under pre-AIPA 35 U.S.C. § 102(e), the U.S. patent issued from this international application has a 102(e) date as of its US filing date, i.e., August 8, 2001. Under the pre-AIPA, the WIPO publication date does not qualify as a 102(e) date; the publication date can only be applied under 35 U.S.C. §§ 102(a) or (b). As shown in the diagram above, the present application claims domestic priority back to May 9, 2000, which is earlier than the publication date of PCT/EP00/00958. As such, no 102 rejection may be applied to the present application and applicants request that this rejection be withdrawn.

Obviousness-type Double Patenting:

Claims 1-9 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-15 and 1-5 of US 6,455,524 and 6,630,466 respectively. Applicants will file terminal disclaimers to overcome the nonstatutory obviousness-type double patenting rejections over US 6,455,524 and 6,630,466, at the conclusion of prosecution of this case, should that become necessary.

Appl. No. 10/608,753
Reply dated November 29, 2007
Reply to Office Action of May 30, 2007

In view of the above amendments and remarks, applicants respectfully submit that this application is now in condition for allowance and earnestly request such action. If any points remain at issue which can best be resolved by way of a telephonic or personal interview, the Examiner is kindly requested to contact the undersigned attorney at the telephone number listed below.

Respectfully submitted,

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Attachment – Copy of Walland Declaration